

edges of the array as a whole. This field has a gradient that results in a force on the magnetic particles. According to certain embodiments of the invention such an effect can be minimized by including a flux circulator in the magnetic device, as pictured in **FIG. 14**. The flux circulator may comprise a loop that extends around the edges of the chip, allowing the magnetic field lines to circulate therein. The flux circulator may comprise a magnetic material, e.g., cobalt, and can be readily fabricated using the same techniques as those used to fabricate the other elements of the device. Thus the invention may include a flux circulator. In certain embodiments of the invention the flux circulator extends around the edges of the magnetic chip and connects opposite poles of the magnetic regions as depicted in **FIG. 14**.

[0104] (6) Array of Arrays

[0105] The magnetic chip can comprise a plurality of individual arrays or subarrays of attachment locations. Such an arrangement of multiple subarrays is referred to as an array of arrays configuration. The subarrays can be (but need not be) present in a regular arrangement, as shown in **FIG. 8**, which is a fluorescence image obtained (after arraying fluorescently labeled beads) from a 10×10 array of arrays, where each of the 100 subarrays contains a 30×30 pattern of magnetic islands. The individual subarrays can be separated, e.g., by hydrophobic boundaries or by components of a bonded microfluidic assembly.

[0106] The overall layout of the chip may be determined by the study size. For instance, a genotyping study involving relatively few markers (probes) and many samples, e.g., 100 markers and 1000 samples to be analyzed may advantageously employ a chip layout where there are approximately 1000 sites per subarray (providing 10-fold redundancy) and a 1000 array of arrays chip design. This design would allow each sample (e.g., a sample from a single individual) to be interrogated in its own array simultaneously. A study which involves more markers with fewer samples may advantageously employ a chip layout where there are approximately 10,000 sites per array with fewer individual subarrays. When an array of arrays configuration is used a microfluidic assembly is convenient for introducing different bead populations and/or samples to each of the subarrays.

[0107] **FIG. 9** shows an image of an entire magnetic wafer patterned with an array of subarrays. The chip is approximately 3 inches in diameter and contains well over 500 subarrays at a spacing of approximately 0.1 inch in each direction. Each subarray (details not visible in image) contains a 30×30 pattern of magnetic islands such as those shown in the AFM image of **FIG. 6**. Thus each subarray contains approximately 900 attachment sites. An experiment involving the analysis of 100 genomic markers on each of 500 different individuals could be performed in one run on this wafer (assuming 9-fold redundancy).

[0108] (7) Alternative Designs

[0109] It will be appreciated that a number of alternative design approaches are possible and fall within the scope of the invention. For example, a substrate having magnetic regions and nonmagnetic islands could also be used. In such a design one or more surfaces of the gap between the islands comprises or sits above a magnetic material, thereby forming a magnetic well in which a magnetic particle can be

trapped. Alternatively, a flat substrate comprising magnetic and nonmagnetic materials could be used. In some embodiments of the invention the magnetic material regions need not be separated with a nonmagnetic material. For example, the surface of the chip may be similar to a computer hard disk, having a pattern of magnetization written on it such as those used to indicate 0's and 1's on a hard disk. The areas of 0's and 1's can be provided in a conventional fashion.

[0110] According to certain embodiments, the localized magnetic fields extend between opposite poles of individual magnetic regions rather than between opposite poles of adjacent magnetic regions. **FIG. 15** shows a schematic view of such a chip design employing localized magnetic fields extending between opposite poles of individual magnetic regions having a circular cross-section. On this figure, magnetization is in the z-axis, i.e., perpendicular to the plane of the paper. In those embodiments of the invention in which localized magnetic fields extend between opposite poles of single magnetic regions rather than between opposite poles of two magnetic regions, the descriptions herein that refer to the space, region, or volume between two magnetic regions generally apply to the volume between opposite poles of a single magnetic region where relevant in the context of the description.

[0111] While varying in configuration, the embodiments described above incorporate the common feature of producing localized magnetic fields within or between magnetic regions, where the localized magnetic fields are sufficient to immobilize (trap) a magnetic particle. In other words, the localized magnetic fields produce forces that are of sufficient strength to result in a trapping energy that is significantly greater than the thermal energy of the particle (e.g., 2-fold greater, 3-fold greater, 5-fold greater, 10-fold greater, 100-fold greater, 1,000-fold greater, 10,000-fold greater, etc.), so that thermal motion (diffusion) has essentially no impact on the bead position once it is trapped by the field. Trapping energy is discussed further below.

[0112] B. Materials

[0113] (1) Substrate

[0114] Any of a variety of materials may be used for the substrate. In embodiments of the invention where the substrate is nonmagnetic, silicon is a convenient choice. Other suitable materials include ceramics, glass, metals such as platinum or gold, or polymeric materials such as plastics. In certain embodiments of the invention it may be desirable to fabricate the substrate from a transparent material or to incorporate a transparent material (e.g., glass or plastic) into the substrate beneath the gap regions to allow optical detection from underneath the fabricated chip. In certain embodiments of the invention, e.g., for applications involving biomolecules, it is desirable that regions of the chip that will contact probe and/or target be biocompatible. If a non-biocompatible material is used, it may be coated with a suitable biocompatible material.

[0115] (2) Magnetic Regions

[0116] In certain embodiments of the invention the magnetic regions are made of or comprise a ferromagnetic material such as cobalt. Other ferromagnetic materials such as magnetizable ceramics, iron, nickel, or nickel-iron alloys could also be used. However, since iron or ferrite is toxic to certain biomolecules such as DNA, it is desirable to coat